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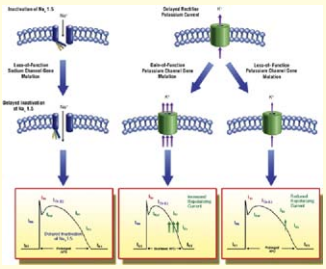
QUARTERLY FOCUS ISSUE: HEART RHYTHM DISORDERS



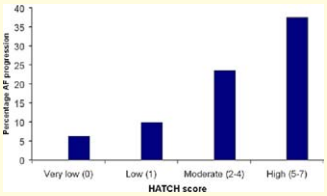
STATE-OF-THE-ART PAPER

SYNCOPE

(continued on page A-23)

ATRIAL FIBRILLATION

HATCH Score Predicts Which Patients Will Advance From Paroxysmal to Sustained AF 725



Cees B. de Vos, Ron Pisters, Robby Nieuwlaat, Martin H. Prins, Robert G. Tieleman, Robert-Jan S. Coelen, Antonius C. van den Heijkant, Maurits A. Allessie, Harry J. G. M. Crijns

de Vos and colleagues investigated which clinical factors would predict whether patients with paroxysmal atrial fibrillation (AF) would develop a more sustained form of AF in the next year. Multivariate analysis showed that heart failure, age, previous transient ischemic attack (TIA) or stroke, chronic obstructive pulmonary disease, and hypertension were independent predictors of AF progression. These risk factors were combined into the HATCH score, with 2 points for a history of heart failure and stroke or TIA. Nearly 50% of the patients with a HATCH score >5 progressed to persistent AF versus 6% of the patients with a HATCH score of 0.

Editorial Comment: Arshad Jahangir, Shishir Murarka, p. 732

ATRIAL FIBRILLATION

The Risks/Benefits of Oral Anticoagulation After Successful AF Ablation 735

Sakis Themistoclakis, Andrea Corrado, Francis E. Marchlinski, Pierre Jais, Erica Zado, Antonio Rossillo, Luigi Di Biase, Robert A. Schweikert, Walid I. Saliba, Rodney Horton, Prasant Mohanty, Dimpi Patel, David J. Burkhardt, Oussama M. Wazni, Aldo Bonso, David J. Callans, Michel Haissaguerre, Antonio Raviele, Andrea Natale

Pulmonary vein isolation is an effective treatment for atrial fibrillation (AF), but little is known about the subsequent risk of thromboembolism and thus the utility of continuing oral anticoagulation (OAT). Themistoclakis and colleagues studied more than 3,000 patients, of whom ~80% discontinued OAT 3 to 6 months after ablation (Off-OAT group), while the other 20% remained on OAT (On-OAT group). During the 2-year follow-up, 0.07% of Off-OAT group patients and 0.45% of On-OAT patients had an ischemic stroke. A major hemorrhage occurred in 1 Off-OAT patient and in 13 On-OAT patients. In this nonrandomized study, the risk–benefit ratio favors the suspension of OAT after successful AF ablation even in patients with a $CHADS_2$ risk score of ≥2.

Editorial Comment: Ivan Cakulev, Albert L. Waldo, p. 744

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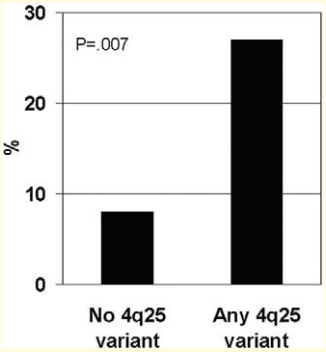


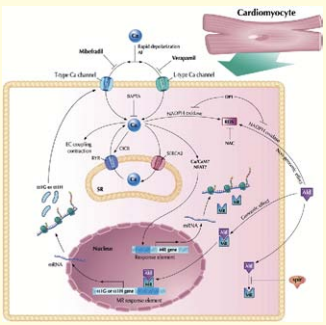
ATRIAL FIBRILLATION

Chromosome 4q25 Variants Linked to AF Recurrence After Ablation **747**

Daniela Husser, Volker Adams, Christopher Piorkowski, Gerhard Hindricks, Andreas Bollmann

Recent studies have identified 2 single nucleotide polymorphisms on chromosome 4q25 as possibly related to atrial fibrillation (AF). This chromosomal location is in a noncoding region but is close to the gene *PITX2*, which is important for myocardium development in the pulmonary veins. Husser and colleagues genotyped almost 200 subjects who underwent AF catheter ablation and then performed serial 7-day Holter electrocardiogram recordings to detect AF recurrences. The presence of either variant allele doubled the risk for early AF recurrence (within the first 7 days) and more than quadrupled the risk for late AF recurrence (within 6 months). Polymorphisms on chromosome 4q25 modulate the risk for AF recurrence after catheter ablation.

Editorial Comment: Jennifer L. Hall, Ana Barac, Emelia J. Benjamin, p. 754



ATRIAL FIBRILLATION

Aldosterone May Underlie Atrial Ionic Remodeling During AF **758**

Chia-Ti Tsai, Fu-Tien Chiang, Chuen-Den Tseng, Juey-Jen Hwang, Kuan-Ting Kuo, Cho-Kai Wu, Chih-Chieh Yu, Yi-Chih Wang, Ling-Ping Lai, Jiunn-Lee Lin

Tsai and colleagues studied the role of steroidogenesis proteins and aldosterone in the atrium, and their possible role in triggering or maintaining atrial fibrillation (AF). Patients with AF had significantly higher atrial mineralocorticoid receptor (MR) expression compared with those with normal sinus rhythm. Rapid depolarization, mimicking AF, increased MR expression in a cellular model through a calcium-dependent mechanism. Aldosterone increased oxidative stress in these cells and increased the number of T-type calcium channels, which led to increased intracellular calcium load. These results help to identify the role of aldosterone and MR in the atrial remodeling that occurs during AF.

Editorial Comment: Panagiotis Korantzopoulos, John A. Goudevenos, p. 771

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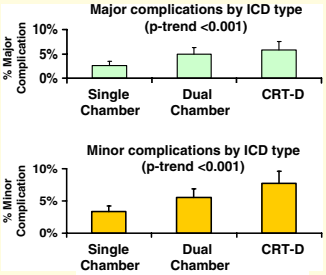


IMPLANTABLE CARDIOVERTER-DEFIBRILLATORS

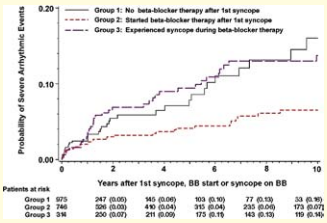
Frequency of Complications After Defibrillator Implantation 774

Douglas S. Lee, Andrew D. Krahn, Jeffrey S. Healey, David Birnie, Eugene Crystal, Paul Dorian, Christopher S. Simpson, Yaariv Khaykin, Douglas Cameron, Amir Janmohamed, Raymond Yee, Peter C. Austin, Zhongliang Chen, Judy Hardy, Jack V. Tu, for the Investigators of the Ontario ICD Database

Lee and colleagues used a mandated registry of all newly-implanted cardioverter-defibrillators (ICDs) at 18 centers to determine the rate of early complications after these procedures. Major complications occurred in 4.1% of de novo procedures. Compared with those implanted with a single-chamber device, implantation of a cardiac resynchronization therapy defibrillator (CRT-D) (adjusted hazard ratio [HR]: 2.2) or dual-chamber device (HR: 1.8) increased the risk of major complications. Major complications were those that required a subsequent procedure, hospitalization, substantive parenteral therapy, or death. Complications after ICD implantation are strongly associated with device type; these complications also increase the risk of death.

LONG QT SYNDROME

Patients With LQTS Who Experience Syncope While Taking Beta-Blockers Are at High Risk for Subsequent Events 783

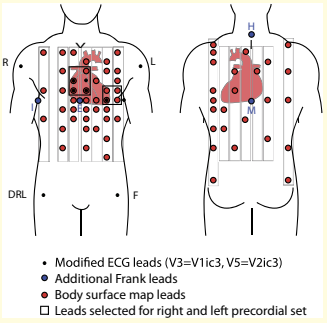


Christian Jons, Arthur J. Moss, Ilan Goldenberg, Judy Liu, Scott McNitt, Wojciech Zareba, Ming Qi, Jennifer L. Robinson

While syncope is known to predict future fatal arrhythmias in patients with long QT syndrome (LQTS), there is no data regarding risk stratification for LQTS patients who initially present with syncope. More than 1,000 patients presenting with syncope as a first symptom were drawn from the International LQTS Registry. The main end point was a severe arrhythmic event (SAE) comprising aborted cardiac arrest, appropriate implantable cardioverter-defibrillator therapy, and sudden cardiac death. The lowest risk for SAEs was in patients with only 1 syncopal episode before starting beta-blocker therapy. Patients experiencing syncope while on beta-blockers had a 3.6-fold increased risk for SAEs relative to the low-risk group. LQTS patients with syncope during beta-blocker therapy are at high risk for life-threatening events, and ICD therapy should be considered.

BRUGADA SYNDROME

ECG Abnormalities Seen in Brugada Syndrome Localize to the Right Ventricle 789



Pieter G. Postema, Pascal F. H. M. van Dessel, Jan A. Kors, Andre C. Linnenbank, Gerard van Herpen, Henk J. Ritsema van Eck, Nan van Geloven, Jacques M. T. de Bakker, Arthur A. M. Wilde, Hanno L. Tan

Postema and colleagues studied changes in various electrocardiographic depolarization and/or repolarization variables that produce the type 1 Brugada Syndrome (BrS) electrocardiogram (ECG) during ajmaline provocation testing. Simultaneous recordings of ECG, vectorcardiogram, and body surface potential maps were obtained. The type 1 ECG was caused by right terminal conduction delay in combination with an increase in late potentials in the right precordial leads, but not with repolarization abnormalities. The type 1 BrS ECG is caused predominantly by localized depolarization abnormalities in the right ventricle.

Editorial Comment: Martin Borggrefe, Rainer Schimpf, p. 798

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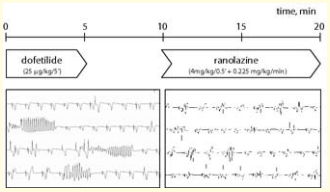


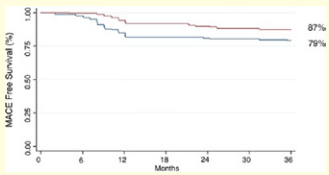
INTERVENTIONAL CARDIOLOGY

TORSADE DE POINTES

Ranolazine Reduces Torsades de Pointes in a Dog Model **801**

Gudrun Antoons, Avram Oros, Jet D. M. Beekman, Markus A. Engelen, Marien J. C. Houtman, Luiz Belardinelli, Milan Stengl, Marc A. Vos

Antoons and colleagues investigated whether ranolazine reduces dofetilide-induced torsades de pointes (TdP) in a model of long QT syndrome: the dog with chronic atrioventricular block (cAVB). Ranolazine reduced the number of TdP episodes and partially reversed the increase of beat-to-beat variability of repolarization without affecting the dofetilide-induced QT prolongation. In cAVB myocytes, ranolazine suppressed dofetilide-induced early after depolarizations. The antiarrhythmic activity of ranolazine in cAVB dogs appears to be through reduced late Na^+ current; these results help us to understand the antiarrhythmic effects of ranolazine.



INTERVENTIONAL CARDIOLOGY

SES Safely Reduces the Rate of TLR Post-STEMI Compared With BMS **810**

Roberto Violini, Carmine Musto, Francesco De Felice, Marco Stefano Nazzaro, Alberta Cifarelli, Tommasangelo Petitti, Rosario Fiorilli

The SESAMI (Sirolimus-Eluting Stent Versus Bare-Metal Stent In Acute Myocardial Infarction) trial randomized 320 ST-segment elevation myocardial infarction (STEMI) patients to either a sirolimus-eluting stent (SES) or a bare-metal stent (BMS). Previously reported 1-year outcomes showed reduced rates of target lesion revascularization (TLR) with SES. This report by Violini and colleagues extends the follow-up period to 3 years, which is important given the concern for possibly higher rates of stent thrombosis (ST) with SES after stopping clopidogrel. The 3-year incidence of major adverse cardiovascular events (MACE) was lower in the SES group compared with the BMS group (12.5% vs. 21%), driven primarily by reduced TLR. The cumulative incidence of death and re-myocardial infarction, starting from clopidogrel discontinuation, was comparable in the 2 groups, with no evidence of higher rates of ST with SES. The clinical benefits of SES over BMS for STEMI patients are maintained at 3 years in this randomized trial.

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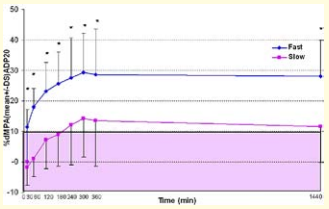
ANTIPLATELET THERAPY



ANTIPLATELET THERAPY

Slow Response Predicts Low Response for Clopidogrel **815**

Anne Bellemain-Appaix, Gilles Montalescot, Johanne Silvain, Olivier Barthélémy, Farzin Beygui, Jean-Philippe Collet, Georges Sideris, Catherine Meuleman, Claire Bal-dit-Sollier, Nicolas Lellouche, Grégory Ducrocq, Michel Slama, Olivier Milleron, Patrick Henry, Ludovic Drouet, for the ALBION Investigators

This post-hoc analysis of the ALBION (Assessment of the Best Loading Dose of Clopidogrel to Blunt Platelet Activation, Inflammation and Ongoing Necrosis) study assessed early kinetic profiles of adenosine diphosphate-induced maximal platelet aggregation (MPA) and ΔMPA, with measurements at 8 time points during the 24 h after clopidogrel loading (300, 600, or 900 mg). Low response was defined as ΔMPA <10% and fast response as ΔMPA ≥10% within the first hour after loading. Fifty-five percent of subjects were slow responders, and these subjects were twice as likely to have high post-treatment platelet reactivity. The response to clopidogrel within the first hour of administration is a reliable marker of the final clopidogrel response.

HYPERTROPHIC CARDIOMYOPATHY

HYPERTROPHIC CARDIOMYOPATHY

Meta-Analysis of Septal Alcohol Ablation Compared With Septal Myectomy **823**

Shikhar Agarwal, E. Murat Tuzcu, Milind Y. Desai, Nicholas Smedira, Harry M. Lever, Bruce Lytle, Samir R. Kapadia

Agarwal and colleagues performed a systematic review and meta-analysis of 12 studies comparing outcomes of septal ablation (SA) and septal myectomy (SM) for the treatment of hypertrophic obstructive cardiomyopathy (HOCM). No significant differences between short- and long-term mortality were found. In addition, no significant differences were found in post-intervention functional status, ventricular arrhythmia occurrence, reinterventions performed, and post-procedure mitral regurgitation. However, SA was associated with a 2.6-times higher risk for permanent pacemaker implantation. Both SA and SM are effective treatments for HOCM; the preferred procedure for an individual patient will depend on available resources and informed decision making.